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Prioritising research challenges and funding for allergy and asthma and the need for translational research - the European Strategic Forum on Allergic Diseases

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Abstract

The European Academy of Allergy and Clinical Immunology (EAACI) organised the first European Strategic Forum on Allergic Diseases and Asthma. The main aim was to bring together all relevant stakeholders and decision-makers in the field of allergy, asthma and clinical Immunology around an open debate on contemporary challenges and potential solutions for the next decade. The Strategic Forum was an upscaling of the EAACI White Paper aiming to integrate the Academy's output with the perspective offered by EAACI's partners. This collaboration is fundamental for adapting and integrating allergy and asthma care into the context of real-world problems. The Strategic Forum on Allergic Diseases brought together all partners who have the drive and the influence to make positive change: National and International Societies, patients' organisations, regulatory bodies and industry representatives. An open debate with a special focus on drug development and biomedical engineering, big data and information technology and allergic diseases and asthma in the context of environmental health concluded that connecting science with the transformation of care and a joint agreement between all partners on priorities and needs are essential to ensure a better management of allergic diseases and asthma in the advent of precision medicine together with global access to innovative and affordable diagnostics and therapeutics.

Key words: asthma, allergic diseases, big data, environmental health, exposome, implementation science, quality criteria, translational research

Abbreviations

CMDh = Co-ordination Group for Mutual Recognition and Decentralised procedures - Human
CME = continuous medical education
COPD = chronic obstructive lung disease
CPD = continuous professional development
EAACI = European Academy of Allergy and Clinical Immunology
EFA = European Federation of Allergy and Airways Diseases Patients' Associations
EMA = European Medicine Agency
EPA/UNEPSA = European Pediatric Association
ERS = European Respiratory Society
ESID = European Society for Immunodeficiencies
ETRs = European Training Requirements
EU = European Union
GARD = The Global Alliance against Chronic Respiratory Diseases
HTA = health technology assessment
INSERM = The French National Institute of Health and Medical Research
MDGs = Millennium Development Goals
NCDs = non-communicable diseases
PEI = Paul Ehrlich Institute
PID = primary immune deficiencies
SDGs = Sustainable Development Goals
UEMS = Union Européenne des Médecins Spécialistes
UN = United Nations
WHO = World Health Organisation

Introduction

Allergic diseases and asthma represent one of the most frequent chronic diseases worldwide encurring a significant economic burden and impairment in the quality of life (table 1) [1].

Table 1 : key epidemiologic data for the major allergic diseases

		Reference
Asthma	339.4 million people worldwide affected by asthma. 3.6% increase in age-standardised prevalence since 2006 23.7 million DALYs globally. 23rd (global) and 31st (LMICs) among the leading causes of premature mortality	2016, the Global Burden of Disease study
Allergic rhinitis	Affects up to 40% of the population worldwide. High prevalence in the developed nations of the Northern Hemisphere, with 23-30% affected population in Europe and 12-30% in the USA. Great diversity of prevalence in the non-Western populations of the Southern Hemisphere, with wide inter- and intra-regional	EAACI Global Atlas of Allergic rhinitis and chronic rhinosinusitis 2016

	variations ranging from 2.9% to 54.1% between countries.	
Atopic dermatitis	Point prevalence in adults in the overall/treated populations was 4.9%/3.9% in the US, 3.5%/2.6% in Canada, 4.4%/3.5% in the EU, and 2.1%/1.5% in Japan. 15-20% of children; the incidence has in-creased by 2- to 3-fold during the past decades in industrialized countries. Continues to increase in prevalence, specifically in young children (age 6-7 as compared to age 13-14 years) and in low-income countries, such as Latin America or South East Asia	Barbarot S, et al. Allergy. 2018;73(6):1284-1293 ISAAC phase I and III
Food allergy	In Western countries, challenge-diagnosed food allergy reported to be as high as 10%, with the greatest prevalence noted among younger children. There is also growing evidence of increasing prevalence in developing countries, with rates of challenge-diagnosed food allergy in China and Africa reported to be similar to that in Western countries.	Loh and Tang, Int J Environ Res Public Health. 2018 ; 15(9): 2043.
Drug allergy	True prevalence unknown The majority of currently available epidemiologic studies report adverse drug reactions which account for 3 to 6% of all hospital admissions and occur in 10 to 15% of hospitalized patients 8.3% (range across studies 0.7-38.5%) self-reported drug allergy.	Thong and Tan, Br J Clin Pharmacol. 2011; 71(5): 684–700 Sousa-Pinto, Ann Allergy Asthma Immunol. 2017;119(4):362-373

On 17 November 2018 the European Academy of Allergy and Clinical Immunology (EAACI) organised the first European Strategic Forum on Allergic Diseases and Asthma in Zurich, Switzerland. The main aim was to bring together all relevant stakeholders and decision-makers in the field of allergy, asthma and clinical immunology around an open debate on contemporary challenges and potential solutions for the next decade. The Strategic Forum is an upscaling of the EAACI White Paper [1], launched in May 2018, a collaborative effort of the EAACI family, Sections, Interest Groups and Working Groups and patients' organisations, offering a critical view on the allergic diseases and asthma landscape in Europe together with an informed analysis of future trends and needs, while identifying and promoting research priorities in allergy, asthma and clinical immunology, setting the standards and quality criteria and providing guidance and training for practice and research.

Allergic diseases and asthma management – the power of partnership

All EAACI stakeholders are key companions actively involved in all EAACI platforms, from development and implementation of the EAACI scientific and educational output to joint advocacy efforts. Working together with National and International Societies, patients' organisations, regulatory bodies and industry representatives is crucial for promoting good clinical practice, high standards of education and outstanding research within Europe and worldwide. Our partners' perspective is fundamental for adapting and integrating the Academy's output into the context of real-world problems.

World Health Organisation (WHO): According to WHO non-communicable diseases (NCDs) such as diabetes, cancer and heart diseases are one of the ten threats for global health in 2019 and are responsible for 70% of deaths worldwide. The collaboration of academic institutions is critical for the implementation of WHO's public health guidelines mandate. Joint activities will improve management of allergic diseases and asthma and reduce the burden of the disease together with more efficient use of limited resources. The consumption of a healthy diet and achievement of an excellent nutritional outcomes is vital for all populations at all stages of the life course, influencing metabolic and immunological reactions.

1. Breastfeeding has a major role in the prevention of atopic dermatitis, asthma, allergic rhinitis and food allergies [2,3]. The promotion, protection and support of exclusive breastfeeding should be a key element of the public health strategies of all countries to reach the target of at least 50% exclusive breastfeeding by 2025 globally [4].
2. There is increasing public concern on food allergies. Allergen labelling has been established for food products and menus [5]. Discouraging self-diagnosis and the consumption of unhealthy diets are important preventive and public health actions. Correct information to the public and counselling by primary health care professionals will be essential [6]. The role of EAACI in promoting good clinical practice would be particularly welcome.
3. Research in clinical immunology contributes to a better understanding of the role of different nutrients and foods in modulating the immune response and further help the definition of healthy diets [7,8,9].

Paul Ehrlich Institute (PEI): A large amount of clinical data for allergen immunotherapy (AIT) products has been generated in recent years. Thus, it is possible to move towards the state-of-the-art evidence for safety and efficacy.

1. In 2015 European Medicines Agency (EMA) recognised that there is severe heterogeneity in the way allergen products are regulated within the European Union (EU), as it is unclear for individual member states which products are on the market in which country, which regulatory approach is followed and which requirements are demanded for the products [10,11].
2. During the harmonisation of regulatory approval for allergen immunotherapy two major problems were identified: regulatory and procedural issues (e.g. on authorisation process, named patient product availability, umbrella authorisation, mixed applications) and scientific issues (adequacy in requirements on quality, safety and efficacy for rare allergens) [12,13,14]. The Co-ordination Group for Mutual Recognition and Decentralised procedures - Human (CMDh) is developing an overarching guideline to support harmonisation across EU Member States while the Rheumatology/Immunology Working Party/Committee for Medicinal Products for Human Use is producing a concept paper (potentially followed by a guideline) for allergen products intended for allergies with low prevalence [15,16].

The European Union of Medical Specialists (Union Européenne des Médecins Spécialistes (UEMS): Differences in healthcare systems can impact on the mobility of professionals and patients, and require harmonisation within European states. There are several strategic areas ensuring harmonisation for the management of allergic diseases:

1. Training of specialists with 3 key pillars: European Training Requirements (ETRs), European Assessments (Examinations) and Visitation of Training Centres. The UEMS Council approved the European Programme for training in clinical allergology. EAACI and UEMS offer a common written exam, the EAACI-UEMS Knowledge test, that is revised and certified also by an external professional institution, the Institute of Medical Examination in Berne, Switzerland (IML)
2. CME (continuous medical education) and CPD (continuous professional development). The European Council on CPD is meant to bring together all the constituents which work closely with international licensing and accreditation authorities, and on the other side UEMS sections and boards as well as European scientific societies. This discussion forum started in October 2017 last year and is organised each year with the aim to solve several areas of overlap between the CME and the medical training and licensing.
3. Quality assurance in medical practice. The UEMS model is to ensure that the medical profession retains the responsibility for the key pillars supporting high quality of care: medical regulation, certification and registration, education, fitness to practice, standards and ethics.

To support the best training and delivery of high-standard care for allergic diseases and asthma the UEMS Section and Board on Allergology together with EAACI advocates the status of a full specialty of allergology in each European country [17,18].

The European Federation of Allergy and Airways Diseases Patients' Associations (EFA): The crucial role of patient involvement is fully recognised today and there have been great strides in the promotion and organisation of self-management [19,20,21,22]. However, the progress is patchy, participation is resourced unequally, there is not sufficient investment in the prevention for allergy and asthma and no coordinated preventative advice for patients. In addition, food allergen thresholds and labelling regulations need further implementation, there is confusion on consumer choice and patient needs and scarce research community interest. The following key pillars support EFA advocacy efforts to improve the lives of people with allergy and asthma:

1. Prevention through healthy environments and lifestyle focusing on the quality of indoor and outdoor air, precautionary labelling of food allergens, patients as “food detectives”, tobacco ban, chemicals exposure regulation, etc.
2. Access to timely and high-quality health and social care, including digital health-care and patients’ involvement in health technology assessment (HTA)
3. Patient participation as individuals but also as patient groups in prevention, care and research through capacity- and patient evidence building
4. Cure through participatory and meaningful research and big data sharing in allergy, asthma and COPD.

The French National Institute of Health and Medical Research (INSERM) considers allergies amongst its priorities due to increasing prevalence and costs.

1. Air pollution, tobacco smoke and ambient temperatures rise due to environmental and climate changes, affecting pollen and moulds counts, and stinging insect numbers are well-known avoidable risk factors for allergic disease [23,24]
2. Intensified multidisciplinary and translational research is needed to elucidate the aetiology of allergic diseases and asthma, underlying mechanisms, treatment, management and cost-benefit of action [1, 25,26]
3. Implementation of the exposome approach incorporating both environmental and socioeconomic determinants of the allergic condition has the potential to enable comprehension of the allergy epidemics and help planning better interventions for prevention or control [27,28]
4. Lobbying for a healthier environment for allergic patients is urgently needed. Adopting and enforcing the WHO standards on chemical air pollution or greenhouses gases to lower their emissions and stop climate change together with measures lowering indoor air pollution, allergen and drug exposures and banning tobacco smoke will certainly help in the near future the management of allergic diseases and asthma.
5. National allergy action plans promoting primary and secondary prevention of allergic diseases are equally top priority

European Respiratory Society (ERS): Healthy lungs are a cornerstone of human health. Globally, respiratory diseases pose an immense worldwide health burden. Five of these diseases, including asthma, are among the most common causes of severe illness and death worldwide. By raising the profile of lung science, education and advocacy we can improve the care for chronic respiratory diseases in Europe and worldwide [29].

1. Encouraging health care provider and patient engagement in a multidisciplinary approach and ensuring that lung health is accessible for all is a major goal to be reached in the near future
2. Healthcare systems should be proactive rather than reactive and ideally, they should include national programmes for all the main respiratory diseases.
3. Comprehensive disease registries and collaborative Pan-European centre-based networks will ensure prospective collection of high-quality real-life data. Stronger surveillance systems are also highly necessary [30, 31,32].
4. Presently, collaboration in Europe lacks a strong strategic scientific framework for tackling chronic diseases. We need a scientific, research and innovation platform in Europe to consolidate expertise and resources across borders, providing significant added value.

European Pediatric Association (EPA/UNEPSA): Over the past few decades the epidemiology of children's health has changed significantly. Global Millennium Development Goals (MDGs) allowed to reduce the under-5 mortality rate (with the smallest reduction of death rate among the 15-19 years old). Sustainable Development Goals (SDGs) shift the efforts towards a holistic, child-right oriented, multisectoral, prevention-based life course approach. Accordingly, the new goal for the professional community is innovative research and evidence-based data collection to help our patients of paediatric age to develop and thrive to achieve their best potential. Child health programming from pre-conception to adolescence and youth years should be the focus of professional paediatric caregivers, community and families living in Europe, adapted to a wide range of diversities in life style, economic status, health care systems, personal beliefs and religions. Academia should lead the way to ensure for all European children equal rights to the highest levels of quality of

care, while harmonising the heterogeneous systems of paediatric care and education across Europe. The following directions were highlighted as essential:

1. Translation of guidelines into clinical practice, big data collection, open collaboration and cooperation, join audit programmes and quality criteria are essential to improve the quality of care for pediatric patients with allergic diseases and asthma [33,34,35].
2. New technologies will provide an opportunity to improve allergic diseases control and quality of life of both the patient and family members, and reduce the frequency of exacerbations.
3. The “one voice speaking paediatricians and allergists initiative” developed based on harmonised best practice in the management of allergy and asthma for paediatric patients across Europe

European Society for Immunodeficiencies (ESID): Joint initiatives and alliances with societies with common interests and collaboration between clinicians, scientists and patients will ensure better management of patients with immune deficiencies.

1. A novel approach with focus on immune dysregulation not just immunodeficiency is necessary in the near future [36]
2. Registry based studies provide the platform where molecular technologies meet the clinical data for diagnosis & treatment
3. Raising awareness on primary immune deficiencies (PID), providing support for better management, networking to share knowledge & expertise and working closely with nursing & patient groups, enthusing the next generation of leaders in PID practice & research throughout Europe through education and focusing on less well served countries are key pillars for better PID care [37]

The Global Alliance against Chronic Respiratory Diseases (GARD): Preventing and controlling chronic respiratory diseases and keeping them on the global health agenda, will require the ongoing energies of all stakeholders. Thus, the following areas should be prioritised:

1. Support for countries in the format of a network through which collaborating parties combine their strengths, thus achieving results that no partner could obtain alone [38]
2. Asthma and preventable deaths. According to the Global Asthma Report 2018 asthma kills around 1000 people every day and affects as many as 339 million people and prevalence is rising [39]. Low- and middle-income countries disproportionally suffer the most severe cases. Effective treatments for asthma are often unavailable or unaffordable as many governments have overlooked asthma in their plans to address NCDs. Although asthma mortality rates have decreased in many countries over the last decade, avoidable asthma deaths are still occurring due to inappropriate management of asthma. Asthma is a major but remediable global health problem: two of the five interventions adopted by WHO to tackle NCDs – tobacco control, and essential medicines and technologies will directly reduce the worldwide burden of asthma [7]. However, the focus of the United Nations (UN) 2030 Strategic Development Goals on mortality alone does not capture morbidity and the imperative to reduce the worldwide burden of asthma. In addition, asthma monitoring needs to be ongoing and widespread as half of the world’s countries have never studied the prevalence of asthma.

3. There is a need to support the transformation of the health care system with use of mobile Health and self-care, health literacy and for embedding the environment (air pollution, aerobiology) and work/school productivity in the integrated care pathways [40,41].

Research priorities for allergic diseases and asthma

Agreeing on future research priorities in allergic diseases and asthma implies both responsibility and vision. Where and how to best use the diminishing resources of funding bodies and private investors, as well as good coordination of the commitment and efforts of researchers are highly challenging tasks nowadays. It is also difficult to reconcile the predictable development of current research with unpredictable external factors such as new epidemics, new discoveries of our and other disciplines or with changes in the leadership of research in Europe and in the global world of science. Thus, EAACI decided to share this responsibility and vision with a wider Think Tank by defining five research priorities, open to public consultation and input from key opinion leaders from different scientific institutions asking them to prioritise topics selected and to suggest new ones (Table 2) and to call on a Strategic Forum to share its vision with all stakeholders.

Table 2: Outcome of EAACI survey to worldwide key opinion leaders on research priorities for allergic diseases and asthma

Prioritisation of research areas in allergic diseases and asthma 1. Translational research and implementation science 2. Drug development and biomedical engineering 3. Big data and information technology (including mobile health) 4. Allergic diseases and asthma in the context of environmental health 5. The developmental exposome
Additional research challenges emerging from the survey 1. Social and economic impact of allergic diseases 2. Organization of health care services and access to cures 3. The impact of a precision approach 4. Patient participation in health policies and disease management

All topics were discussed during the lively debate at the Strategic Forum with a special focus on drug development and biomedical engineering, big data and information technology and allergic diseases and asthma in the context of environmental health.

Translational research and implementation science

All Forum participants agreed on the key role of translational research fostering the multidirectional and multidisciplinary integration of basic research, patient-oriented research, and population-based research, with the long-term aim of improving the management of allergic diseases and asthma [1,42,43,44, 45,46]. (figure 1). Implementation science was also evaluated as a key tool for identifying all major contributions to health care, from individual factors up to policy and public health interventions. Several effective strategies to implement evidence-based practices such as planning, education, financing, restructuring, quality management, and attention to policy context were highlighted (figure 2). This approach can support the adaptation of the precision medicine approach in a wide range of health care systems facilitating patients access to new drugs or other interventions based on

precise endotyping that poses at present significant problems on the sustainability of the healthcare system [40, 47,48].

Drug development and biomedical engineering

Advanced therapies such as gene therapies, cell and tissue therapies, regenerative medicine, the increasing number of biologicals and biosimilars will soon exceed the number of chemical drugs. These therapies together with the introduction of sophisticated devices and biomedical engineered products, all call for a new approach to drug development, evaluation and monitoring [1,49,50,51,52,53]. The high costs of developing new medicines, the low probability for a new product to fulfil the strict regulatory requirements to obtain market authorization and, finally, the financial constraints of most national health services that cannot afford reimbursement for extremely expensive drugs, represent limiting factors for investments in the pharmaceutical area and patient access to new safe and effective drugs. Standard operational procedures and quality criteria should be harmonized among all countries, including those with an emerging pharmaceutical industrial market such as India and China.

Following a lively debate on how to improve the process of drug development, biomarkers and companion diagnostic for allergic diseases and asthma the participants agreed on several priorities (Table 3). If we think globally we should also consider the low-income countries. Although the governments seek cheap and simple biomarkers which will predict the response we must convince them that the precision medicine approach albeit costly at the first evaluation will prove very rewarding in terms of expenditure by better selection of responders and by reducing adverse events and associated healthcare costs. All world citizens should have access to new safe and effective drugs by developing models that, reducing the risk of investments, eventually reduce the price of new medicines, and by establishing heath policies on the basis of reasonable priorities and social equanimity.

Table 3: Proposed innovative approach for the development of cutting-edge therapies for allergic diseases and asthma – the 5 year plan

1. Early collaboration of all stakeholders in drug development
2. Joint health technology assessment scientific advice
3. Novel standard and quality criteria adapted to the concept of precision medicine
4. Development of validated biomarkers and companion diagnostics that enable the dissection of heterogeneous diseases into well-defined phenotypes and endotypes
5. Adaptive pathways for drug development that allow evaluation and monitoring during the entire life-cycle
6. Different approach in terms of systematic nomenclature of allergic diseases shifted towards new mechanisms instead of description of symptoms

The regulatory tools already exist, so what is needed is better guidance on how to address the precision medicine approach at an operational level while interlinking different aspects. For example, if our community seeks faster development of new drugs we need to prove how this will ensure better translation into clinical practice. The regulators have learned that “the one size fits all” approach is not working so if Academia proposes a cost-effective process for precision medicine that will be working in daily practice, the regulators might accept it.

Big data and information technology

Healthcare is at present largely based on evidence provided by randomised controlled clinical trials and observational/epidemiological data in selected populations. There is however a massive amount of data available from healthcare records, registries, and biobanks whose potential in improving knowledge has not yet been fully explored. The availability of new information technology techniques for collecting, analysing and relating the "big data" provided
by the real world opens new horizons to a new, more comprehensive knowledge. Rapid learning systems can shape vast amounts of "omics" (genomics, proteomics, metabolomics, catalomics, phenomics, etc.) together with collecting "real-world" data unbiased by any pre-selection criteria to support real-time clinical decision support at the point of care leading to harmonised care based on quality criteria. The availability and analysis of big data is expected to open a new era in the computing science, with profound effects also in the area of biology and medicine. Computers will not only be instruments to provide answers by elaborating data on the basis of pre-defined algorithms, but will be able to learn themselves from data analysis (machine learning or artificial intellingence) and to provide solutions on the basis of original algorithms [54-71]. Modern telemonitoring systems combined with artificial intelligence can accurately predict asthma exacerbations with the potential to improve self-management interventions [72-74] (figure 3).

However, big data are quite heterogeneous and come from a large variety of sources [75]. Their quality should be carefully checked and new hypotheses deriving from big data should be experimentally tested before neglecting the actual evidence and adopting new diagnostic and therapeutic approaches. There is clearly a huge job to be done in upskilling the healthcare providers, and it's a matter not only of skills but also of attitudes and culture, which are harder to change. Electronic records linked to multiple and quality assured databases are essential, but there is also a big need for bio-informaticians who can ensure that the data available is of, high-quality, and well managed. In addition, efficient usage of big data requests that industry,
regulatory bodies, scientists and clinicians accept transparency policies which make their data available to the community via open platforms

A significant shift in the doctor-patient relationship is expected with the well-informed patient advocating for their own care and connected in real time with the healthcare provider who is provided with personalised information from patient portals. Artificial Intelligence will certainly favour not only a tremendous progress in medical sciences, but will the creation of a new relationship between humans and machines with relevant implications in ethics and responsibilities of the medical profession. Moreover, big data imply a risk for citizens' and patients 'privacy. This should be protected by adequate regulations and accurate anonymization techniques of individual personal data algorithms [76,77].

Allergic diseases and asthma in the context of environmental health

Natural and man-made environments such as air quality, water and soil, together with all the physical, chemical, biological and social features of our surroundings have a major influence on the control and severity of allergic diseases and asthma [28,78,79]. Although the precision medicine revolution has the potential to transform environmental measures we still have a long way to go to more effectively identify what or whom should be targeted. Some environmental interventions like air quality regulation cannot be targeted to any subgroup, genetic, or otherwise. Others, like breastfeeding, vaccination, antismoking campaigns, exercise, or diets, can be targeted, but they need to prove practical and/or cost efficient. The most efficient prevention strategies would identify those at highest risk of disease following avoidable exposures. However, simply evaluating genetic risks is not sufficient since we need to co-factor the interaction with environment. An improved methodological approach

proving causality instead of associations together with an integrated surveillance network for the environment impact on allergies and asthma are key pillars to move this field forward [28,80,81].

The importance of functional foods and nutraceuticals is expanding globally in terms of scientific services, legal aspects, and marketing strategies for health promotion, reduction of disease, and health care costs [82, 83]. Nonetheless, they are marketed without a prescription and their safety and efficacy is yet to be proven, especially if consumed in supra-dietary doses as nutritional supplements.

Urgent and concerted actions are needed to improve the European legislation on environment control, with a special focus on air quality, tobacco banning, indoor and outdoor pollution, invasive allergenic plants and standard occupational exposure.

All participants agreed on "The One Health concept" evaluating the interconnections between human, environment and animal health and food and water safety is being particular amenable for the prevention and better management of allergic diseases and asthma in the future [84,85].

The developmental exposome

Multifactorial diseases such as allergic diseases and asthma involve the combined effects of genetic factors, development-specific exposures (in utero, early-life and childhood exposures) and the biological responses to those exposures (allostasis) [28,86-95].
Many epidemiological, genetic, environmental, and immune risk factors for allergic diseases and asthma are described, however, distinguishing which risk factors are causal, their mechanism of action and how interaction between these factors initiates disease remains poorly understood. Although it is recognized that up to 90% of allergies and asthma results from development-specific exposure with a secondary role of the genetic background significantly less research is oriented towards describing the developmental exposome. Current barriers to our understanding include the limitations of research during gestation and the perinatal period, inadequacies of animal models in recapitulating the onset of human disease, differences between human and experimental animal developmental stages and difficulties in documenting low dose exposure (limited by the sensitivity of the assay), intermittent exposure (limited by the frequency of testing) and transient exposure (the system should be in place at the time of the exposure).

Both primary prevention based on molecular endotypes and the developmental exposome can be prospectively validated using evidence-based clinical management to improve care across the severity spectrum. Investigators with expertise in molecular biology and exposomics need to engage in research planning with experts in informatics, genetics, clinical, health-economics and drug development experts. User-friendly large datasets will support this cooperation.

The exposomic approach is particularly applicable to the study of environmental causes of allergic diseases and asthma as it provides risk profiles instead of single predictors. However, we still lack validated criteria for selecting the best assay(s) to assess biological response for the research question of interest, easy to implement guidelines for sample collection and standards and quality criteria for repositories and biobanks [28,96].

Patient participation in health policies and disease management

All participants stated their strong belief in the patients' role as equal partners with health professionals in the management of their condition, involved in all steps, from research to daily healthcare. Patients are often active people who can, if adequately supported and according to their individual capabilities and situation, make a difference for the sustainability of environmental policies and healthcare systems [97,98].

The five "Ps" of modern healthcare (patient-centered, prompt, personalised, pathway-oriented, portable) and the 5 "Es" of patient empowerment (education, expertise, equality, experience and engagement) were discussed as corner-stones in implementing better management pathways for allergic diseases and asthma.

Conclusion and future directions

The European Strategic Forum on Allergic Diseases organized by EAACI provided a platform where ideas, thoughts and questions were tackled in an open environment, in full alignment with the EAACI belief that progress happens only by bringing together all partners who have the drive and the influence to make positive change (figure 4).

The One Health approach, integrating the technological progress in different disciplines, the exposomics and cross-omics approach, and system biomedicine, represents a major challenge for research in allergic diseases and asthma. This implies a growing importance of computing science for big data storage and analysis.

Connecting science with the transformation of care is necessary is necessary to ensure that the precision medicine tools will facilitate a better management of allergic diseases and asthma. A special focus is advocated for translational research and implementation science, big data and artificial intelligence, "omics"-technologies facilitating personalised therapeutic and prevention approaches, harmonisation and standardisation of the clinical care pathways, novel training competencies and clinical decision systems, investment into smart E-health and M-health programmes and continuous support for patient participation in health policies and disease management (figure 4).

To ensure that progress in research is reflected into a real advance in healthcare and nothing is "lost in translation", a close collaboration of all stakeholders is needed to define priorities and unmet needs as well as to enable a global access to innovative and affordable diagnostics and therapeutics.

References

1. Agache I, Akdis CA, Chivato T, Hellings P, Hoffman-Sommergruber K, Jutel M, et al. EAACI White Paper on Research, Innovation and Quality Care. Accessed on 14.02.2019 at www.eaaci.org/resources/books/white-paper.html
2. Bion V, Lockett GA, Soto-Ramírez N, Zhang H, Venter C, Karmaus W, et al. Evaluating the efficacy of breastfeeding guidelines on long-term outcomes for allergic disease. Allergy. 2016;71(5):661-70
3. Victora CG, Aluísio J D Barros AJD, França GVA, Horton S, Krasevec J, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet 2016; 387: 475–90
4. https://www.who.int/pmnch/media/news/2016/breastfeeding_brief.pdf. Accessed on 25.02.2019
5. Nwaru BI, Hickstein L, Panesar SS, Roberts G, Muraro A, Sheikh A; EAACI Food Allergy and Anaphylaxis Guidelines Group. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. Allergy. 2014;69(8):992-1007.
6. Muraro A, Agache I, Clark A, Sheikh A, Roberts G, Akdis CA, et al; European Academy of Allergy and Clinical Immunology. EAACI food allergy and anaphylaxis guidelines: managing patients with food allergy in the community. Allergy. 2014;69(8):1046-57.
7. www.who.int. Global action plan for the prevention and control of noncommunicable diseases 2013-2020. Accessed on 25.02.2019
8. Branca F, Lartey A, Oenema S, Aguayo V, Stordalen GA, Richardson R, et al. Transforming the food system to fight non-communicable diseases. BMJ. 2019;364:l296
9. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019 Jan 16. pii: S0140-6736(18)31788-4.
10. Zimmer J, Vieths S, Kaul S. Standardization and Regulation of Allergen Products in the European Union. Curr Allergy Asthma Rep. 2016;16(3):21
11. Bonertz A, Roberts G, Slater JE, Bridgewater J, Rabin RL, Hoefnagel M, et al. Allergen manufacturing and quality aspects for allergen immunotherapy in Europe and the United States: An analysis from the EAACI AIT Guidelines Project. Allergy. 2018;73(4):816-826.
12. Bieber T, Vieths S, Broich K. New opportunities and challenges in the assessment of drugs for atopic diseases. Allergy. 2016;71(12):1662-1665.
13. Kaul S, Zimmer J, Dehus O, Costanzo A, Daas A, Buchheit KH, et al. Standardization of allergen products: 3. Validation of candidate European Pharmacopoeia standard methods for quantification of major birch allergen Bet v 1. Allergy. 2016;71(10):1414-24.
14. Zimmer J, Bonertz A, Vieths S. Quality requirements for allergen extracts and allergoids for allergen immunotherapy. Allergol Immunopathol (Madr). 2017;45 Suppl 1:4-11
15. http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Agendas_and_Minutes/Minutes/2018_03_CMDh_Minutes.pdf, Accessed on 25.02.2019
16. https://www.ema.europa.eu/documents/scientific-guideline/concept-paper-guideline-allergen-products-development-moderate-low-sized-study-populations_en.pdf. Accessed on 25.02.2019
17. de Monchy JG, Demoly P, Akdis CA, Cardona V, Papadopoulos NG, Schmid-Grendelmeier P, et al. Allergology in Europe, the blueprint. Allergy 2013;68(10):1211-8.
18. Gerth van Wijk R, Eguiluz-Gracia I, Gayraud J, Gutermuth J, Hamelmann E, Heffler E, et al. The roadmap for allergology in Europe: The subspecialty of

allergology as "stop-over" on the way to a full specialty. An EAACI position statement. Allergy. 2018 ;73(3):540-548.
19. http://www.efanet.org/annual-report/2017
20. Katsaounou P, Odemyr M, Spranger O, Hyland ME, Kroegel C, et al. Still Fighting for Breath: a patient survey of the challenges and impact of severe asthma. ERJ Open Res. 2018;4(4).
21. http://www.efanet.org/resources/library/3296-severely-asthma-project. Accessed on 25.02.2019
22. Honkoop PJ, Simpson A, Bonini M, et al, MyAirCoach: the use of home-monitoring and mHealth systems to predict deterioration in asthma control and the occurrence of asthma exacerbations; study protocol of an observational study. BMJ Open 2017;7:e013935
23. Sanyal S, Rochereau T, Maesano CN, Com-Ruelle L, Annesi-Maesano I. Long-Term Effect of Outdoor Air Pollution on Mortality and Morbidity: A 12-Year Follow-Up Study for Metropolitan France. Int J Environ Res Public Health. 2018;15(11)
24. D'Amato G, Annesi-Maesano I, Cecchi L, D'Amato M. Latest news on relationship between thunderstorms and respiratory allergy, severe asthma, and deaths for asthma. Allergy. 2019;74(1):9-11.
25. Bousquet J, Anto JM, Akdis M, Auffray C, Keil T, Momas I, et al. Paving the way of systems biology and precision medicine in allergic diseases: the MeDALL success story: Mechanisms of the Development of ALLergy; EU FP7-CP-IP; Project No: 261357; 2010-2015. Allergy. 2016;71(11):1513-1525
26. Walker SM, Akdis C, Dahlen SE, Djukanovic R, Edwards J, Garcia-Marcos L, et al. Building the investment case for asthma R&D: the European Asthma Research and Innovation Partnership argument. Clin Exp Allergy. 2016;46(9):1136-8.
27. Cecchi L, D'Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. J Allergy Clin Immunol. 2018;141(3):846-857.
28. Agache I, Miller R, Gern JE, Hellings PW, Jutel M, Muraro A, Phipatanakul W, Quirce S, Peden D. Emerging concepts and challenges in implementing the exposome paradigm in allergic diseases and asthma. Allergy. 2018 Dec 4. doi: 10.1111/all.13690. [Epub ahead of print]
29. Migliori GB, Bel E, Joos G, Elliott M, Rohde G, Holgate ST, et al.The European Respiratory Society evaluates its 2013-2018 strategic plan implementation. Eur Respir J. 2016;47(3):693-8.
30. Soriano JB, Paton J, Martin Burrieza F, Bill W, Pannetier C, Aliberti S, Adcock IM.The ERS Research Agency: the beginning. Eur Respir J. 2016;47(4):1017-23.
31. Maio S, Baldacci S, Bresciani M, Simoni M, Latorre M, Murgia N, et al. RItA: The Italian severe/uncontrolled asthma registry. Allergy. 2018;73(3):683-695.
32. Liu NM, van Aalderen W, Carlsen KCL, Coleman C, Chalmers JD, Cunningham S, et al. Severe Paediatric Asthma Collaborative in Europe (SPACE): protocol for a European registry. Breathe 2018;14(2):93-98.
33. Kercsmar CM, Sorkness CA, Calatroni A, Gergen PJ, Bloomberg GR, Gruchalla RS, et al; National Institute of Allergy and Infectious Diseases–sponsored Inner-City Asthma Consortium. A computerized decision support tool to implement asthma guidelines for children and adolescents. J Allergy Clin Immunol. 2018 Dec 5. pii: S0091-6749(18)31724-X. [Epub ahead of print]
34. Papadopoulos NG, Custovic A, Cabana MD, Dell SD, Deschildre A, Hedlin G, et al. Pediatric asthma: An unmet need for more effective, focused treatments. Pediatr Allergy Immunol. 2019;30(1):7-16.
35. Vishneva E, Namazova-Baranova LV, Alekseeva A, Levina J, Efendieva K, Tomilova A, et al. The Pediatric Asthma Patient Registry In Implementation Of Long Term Follow Up. Value Health. 2015;18(7):A693.

36. Leiding JW, Ballow M. Precision medicine in the treatment of primary immunodeficiency diseases. Curr Opin Allergy Clin Immunol. 2018;18(2):159-166.
37. Odnoletkova I, Kindle G, Quinti I, Grimbacher B, Knerr V, Gathmann B, et al; Plasma Protein Therapeutics Association (PPTA) Taskforce. The burden of common variable immunodeficiency disorders: a retrospective analysis of the European Society for Immunodeficiency (ESID) registry data. Orphanet J Rare Dis. 2018;13(1):201.
38. To T, Cruz AA, Viegi G, McGihon R, Khaltaev N, Yorgancioglu A, et al. A strategy for measuring health outcomes and evaluating impacts of interventions on asthma and COPD-common chronic respiratory diseases in Global Alliance against Chronic Respiratory Diseases (GARD) countries. J Thorac Dis. 2018;10(8):5170-5177
39. http://globalasthmareport.org
40. Hellings PW, Fokkens WJ, Bachert C, Akdis CA, Bieber T, Agache I, et al. Positioning the principles of precision medicine in care pathways for allergic rhinitis and chronic rhinosinusitis - A EUFOREA-ARIA-EPOS-AIRWAYS ICP statement. Allergy. 2017;72(9):1297-1305.
41. Valiulis A, Bousquet J, Veryga A, Suprun U, Sergeenko D, Cebotari S, et al. Vilnius Declaration on chronic respiratory diseases: multisectoral care pathways embedding guided self-management, mHealth and air pollution in chronic respiratory diseases. Clin Transl Allergy. 2019;9:7.
42. Butler D. Translational research: crossing the valley of death. Nature 2008;453:840-842.
43. Woolf SH. The meaning of translational research and why it matters. JAMA 2008;299:211-213.
44. Bender BG. A bootstrap approach to implementation science. Ann Allergy Asthma Immunol 2016;117:213-216.
45. Cunningham S, Pinnock H.Implementation science takes baby steps in infants with bronchiolitis. Thorax. 2018. pii: thoraxjnl-2017-211455
46. Colborn KL, Helmkamp L, Bender BG, Kwan BM, Schilling LM, Sills MR. Colorado Asthma Toolkit Implementation Improves Some Process Measures of Asthma Care. J Am Board Fam Med. 2019;32(1):37-49
47. Crable EL, Biancarelli D, Walkey AJ, Allen CG, Proctor EK, Drainoni ML.Standardizing an approach to the evaluation of implementation science proposals. Implement Sci. 2018;13(1):71
48. Pinnock H, Barwick M, Carpenter CR, Eldridge S, Grandes G, Griffiths CJ, et al; StaRI Group. Standards for Reporting Implementation Studies (StaRI) Statement. BMJ. 2017;356:i6795.
49. Bonini S, Bonini M. Biosimilars and drug development in immunologic diseases. J Allergy Clin Immunol 2017;139:1461-1464.
50. Rasi G, Bonini S. Innovative medicines; new regulatory procedures for the third millennium. Expert Opin Biol Ther 2015;15:5-8.
51. Barnes PJ, Bonini S, Seeger W, Belvisi MG, Ward B, Holmes A. Barriers to new drug development in respiratory disease. Eur Respir J. 2015;45(5):1197-207
52. Bonini S, Eichler H-G, Wathion N, Rasi G. Transparency and the European Medicines Agency. Sharing of clinical trial data. N Engl J Med 2014;371:2552-2555.
53. Palomares O, Crameri R, Rhyner C. The contribution of biotechnology toward progress in diagnosis, management, and treatment of allergic diseases. Allergy. 2014;69(12):1588-601.
54. Diver S, Brightling CE. Big asthma data: getting bigger and more beautiful? Thorax. 2018;73(4):311-312.
55. Pandey G, Pandey OP, Rogers AJ, Ahsen ME, Hoffman GE, Raby BA, Weiss ST, Schadt EE, Bunyavanich S. A Nasal Brush-based Classifier of Asthma

Identified by Machine Learning Analysis of Nasal RNA Sequence Data. Sci Rep. 2018;8(1):8826
56. Ross MK, Yoon J, van der Schaar A, van der Schaar M. Discovering Pediatric Asthma Phenotypes on the Basis of Response to Controller Medication Using Machine Learning. Ann Am Thorac Soc. 2018;15(1):49-58
57. Ghosh D, Bernstein JA, Khurana Hershey GK, Rothenberg ME, Mersha TB . Leveraging Multilayered "Omics" Data for Atopic Dermatitis: A Road Map to Precision Medicine. Front Immunol. 2018;9:2727
58. Bieber T, Akdis C, Lauener R, Traidl-Hoffmann C, Schmid-Grendelmeier P, Schaeppi G, et al. Global Allergy Forum and 3rd Davos Declaration 2015: Atopic dermatitis/Eczema: challenges and opportunities toward precision medicine. Allergy. 2016;71(5):588-92
59. Nieuwenhuis MA, Siedlinski M, van den Berge M, Granell R, Li X, Niens M, et al. Combining genome-wide association study and lung eQTL analysis provides evidence for novel genes associated with asthma. Allergy. 2016;71(12):1712-1720
60. Loureiro CC, Oliveira AS, Santos M, Rudnitskaya A, Todo-Bom A, Bousquet J, et al. Urinary metabolomic profiling of asthmatics can be related to clinical characteristics. Allergy. 2016;71(9):1362-5.
61. Obeso D, Mera-Berriatua L, Rodríguez-Coira J, Rosace D, Fernández P, Martín-Antoniano IA, et al.Multi-omics analysis points to altered platelet functions in severe food-associated respiratory allergy. Allergy. 2018;73(11):2137-2149.
62. Villaseñor A, Rosace D, Obeso D, Pérez-Gordo M, Chivato T, Barbas C, et al. Allergic asthma: an overview of metabolomic strategies leading to the identification of biomarkers in the field. Clin Exp Allergy. 2017;47(4):442-456.
63. Rodrigo-Muñoz JM, Cañas JA, Sastre B, Rego N, Greif G, Rial M, et al. Asthma diagnosis using integrated analysis of eosinophil microRNAs. Allergy. 2018 Jul 24. doi: 10.1111/all.13570. [Epub ahead of print]
64. Doña I, Jurado-Escobar R, Perkins JR, Ayuso P, Plaza-Serón MC, Pérez-Sánchez N, et al. Eicosanoid mediator profiles in different phenotypes of nonsteroidal anti-inflammatory drug-induced urticaria. Allergy. 2019 Jan 22. doi: 10.1111/all.13725. [Epub ahead of print]
65. Segura-Bedmar I, Colon-Ruiz C, Tejedor-Alonso MA, Moro-Moro M. Predicting of anaphylaxis in big data EMR by exploring machine learning approaches. J Biomed Inform. 2018;87:50-59
66. Bousquet J, Agache I, Anto JM, Bergmann KC, Bachert C, Annesi-Maesano I, et al. Google Trends terms reporting rhinitis and related topics differ in European countries. Allergy. 2017;72(8):1261-1266
67. Bonini M. Electronic health (e-Health): emerging role in asthma. Curr Opin Pulm Med. 2017;23(1):21-26.
68. Eguiluz-Gracia I, Tay TR, Hew M, Escribese MM, Barber D, O'Hehir RE, Torres MJ. Recent developments and highlights in biomarkers in allergic diseases and asthma. Allergy. 2018;73(12):2290-230
69. Agache I, Rogozea L. Endotypes in allergic diseases. Curr Opin Allergy Clin Immunol. 2018;18(3):177-183
70. Agache I, Strasser DS, Pierlot GM, Farine H, Izuhara K, Akdis CA. Monitoring inflammatory heterogeneity with multiple biomarkers for multidimensional endotyping of asthma. J Allergy Clin Immunol. 2018;141(1):442-445.
71. Muraro A, Lemanske RF Jr, Hellings PW, Akdis CA, Bieber T, Casale TB, et al. Precision medicine in patients with allergic diseases: Airway diseases and atopic dermatitis-PRACTALL document of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology J Allergy Clin Immunol. 2016;137(5):1347-58
72. Finkelstein J, Wood J. Predicting asthma exacerbations using artificial intelligence. Stud Health Technol Inform. 2013;190:56-8.

73. Finkelstein J, Jeong IC. Machine learning approaches to personalize early prediction of asthma exacerbations. Ann N Y Acad Sci. 2017;1387(1):153-165.
74. Honkoop PJ, Simpson A, Bonini M, Snoeck-Stroband JB, Meah S, Fan Chung K, et al. MyAirCoach: the use of home-monitoring and mHealth systems to predict deterioration in asthma control and the occurrence of asthma exacerbations; study protocol of an observational study. BMJ Open. 2017;7(1):e013935.
75. Sukumar SR, Natarajan R, Ferrell RK. Quality of Big Data in health care. Int J Health Care Qual Assur. 2015;28(6):621-34.
76. Hordern V. Data Protection Compliance in the Age of Digital Health. Eur J Health Law. 2016;23(3):248-64.
77. Rumbold JM, Pierscionek B. The Effect of the General Data Protection Regulation on Medical Research. J Med Internet Res. 2017;19(2):e47.
78. Garcia-Larsen V, Del Giacco SR, Moreira A, Bonini M, Charles D, Reeves T, et al. Asthma and dietary intake: an overview of systematic reviews. Allergy. 2016;71(4):433-42
79. Paciência I, Cavaleiro Rufo J, Silva D, Martins C, Mendes F, Farraia M, et al. Exposure to indoor endocrine disrupting chemicals and childhood asthma and obesity. Allergy. 2019 Feb 11. doi: 10.1111/all.13740. [Epub ahead of print]
80. Steckling N, Gotti A, Bose-O'Reilly S, Chapizanis D, Costopoulou D, De Vocht F, et al. Biomarkers of exposure in environment-wide association studies - Opportunities to decode the exposome using human biomonitoring data. Environ Res. 2018;164:597-624.
81. Krautenbacher N, Flach N, Böck A, Laubhahn K, Laimighofer M, Theis FJ, et al. A strategy for high-dimensional multivariable analysis classifies childhood asthma phenotypes from genetic, immunological and environmental factors. Allergy. 2019 Feb 9. doi: 10.1111/all.13745. [Epub ahead of print]
82. Venter C, Meyer RW, Nwaru BI, Roduit C, Untersmayr E, Adel-Patient K, et al. EAACI Position Paper: Influence of Dietary Fatty Acids on Asthma, Food Allergy and Atopic Dermatitis. Allergy. 2019 Apr 29. doi: 10.1111/all.13764. [Epub ahead of print]
83. Wickens K, Barthow C, Mitchell EA, Kang J, van Zyl N, Purdie G, et al. Effects of Lactobacillus rhamnosus HN001 in early life on the cumulative prevalence of allergic disease to 11 years. Pediatr Allergy Immunol. 2018;29(8):808-814.
84. Lerner H, Berg C. The concept of health in One Health and some practical implications for research and education: what is One Health? Infection ecology & epidemiology. 2015;5:25300
85. Xie T, Liu W, Anderson BD, Liu X, Gray GC. A system dynamics approach to understanding the One Health concept. PLoS One. 2017;12(9):e0184430.
86. Khan SJ, Dharmage SC, Matheson MC, Gurrin LC. Is the atopic march related to confounding by genetics and early-life environment? A systematic review of sibship and twin data. Allergy. 2018;73(1):17-28.
87. Lockett GA, Soto-Ramírez N, Ray MA, Everson TM, Xu CJ, Patil VK, et al. Association of season of birth with DNA methylation and allergic disease. Allergy. 2016;71(9):1314-24.
88. Savage JH, Lee-Sarwar KA, Sordillo J, Bunyavanich S, Zhou Y, O'Connor G, et al. A prospective microbiome-wide association study of food sensitization and food allergy in early childhood. Allergy. 2018;73(1):145-152.
89. Jatzlauk G, Bartel S, Heine H, Schloter M, Krauss-Etschmann S. Influences of environmental bacteria and their metabolites on allergies, asthma, and host microbiota. Allergy. 2017;72(12):1859-1867.

90. Birzele LT, Depner M, Ege M, Engel M, Kublik S, Bernau C, et al. Environmental and mucosal microbiota and their role in childhood asthma. Allergy. 2017;72(1):109-119
91. Muir AB, Benitez AJ, Dods K, Spergel JM, Fillon SA. Microbiome and its impact on gastrointestinal atopy. Allergy. 2016;71(9):1256-63
92. Lau S, Matricardi PM, Wahn U, Lee YA, Keil T. Allergy and atopy from infancy to adulthood: Messages from the German birth cohort MAS. Ann Allergy Asthma Immunol. 2019;122(1):25-32.
93. Thacher JD, Gruzieva O, Pershagen G, Neuman Å, van Hage M, Wickman M, et al. Parental smoking and development of allergic sensitization from birth to adolescence. Allergy. 2016;71(2):239-48.
94. Fuertes E, Markevych I, Bowatte G, Gruzieva O, Gehring U, Becker A, et al. Residential greenness is differentially associated with childhood allergic rhinitis and aeroallergen sensitization in seven birth cohorts. Allergy. 2016;71(10):1461-71
95. Schröder PC, Illi S, Casaca VI, Lluis A, Böck A, Roduit C et al. A switch in regulatory T cells through farm exposure during immune maturation in childhood. Allergy. 2017;72(4):604-615.
96. Benet M, Albang R, Pinart M, Hohmann C, Tischer CG, Annesi-Maesano I, et al. Integrating Clinical and Epidemiologic Data on Allergic Diseases Across Birth Cohorts: A Harmonization Study in the Mechanisms of the Development of Allergy Project. Am J Epidemiol. 2019;188(2):408-417.
97. Hellings PW, Fokkens WJ, Bachert C, Akdis CA, Bieber T, Agache I, et al; ARIA and EPOS working groups Positioning the principles of precision medicine in care pathways for allergic rhinitis and chronic rhinosinusitis - A EUFOREA-ARIA-EPOS-AIRWAYS ICP statement. Allergy. 2017;72(9):1297-1305.
98. http://www.eu-patient.eu/campaign/PatientsprescribE. Accessed on 25.02.2019

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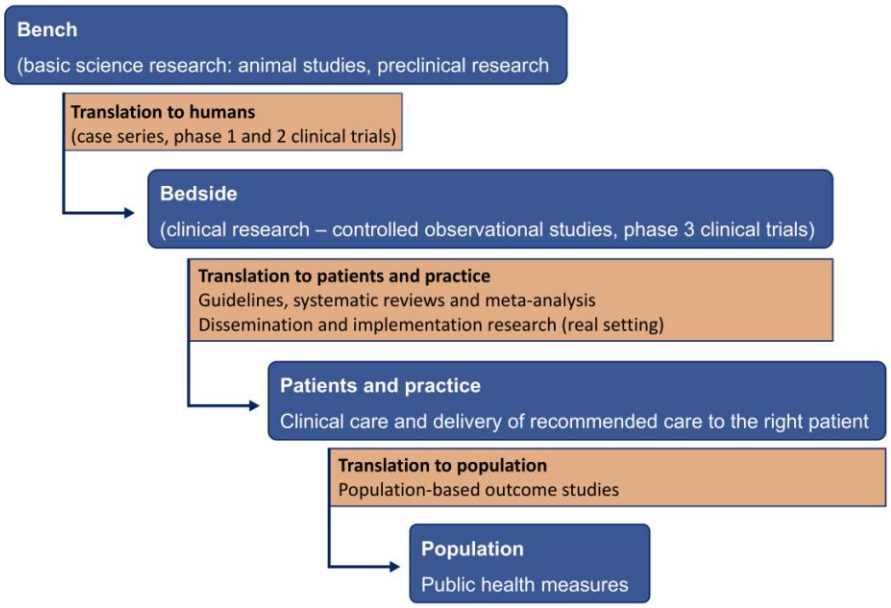
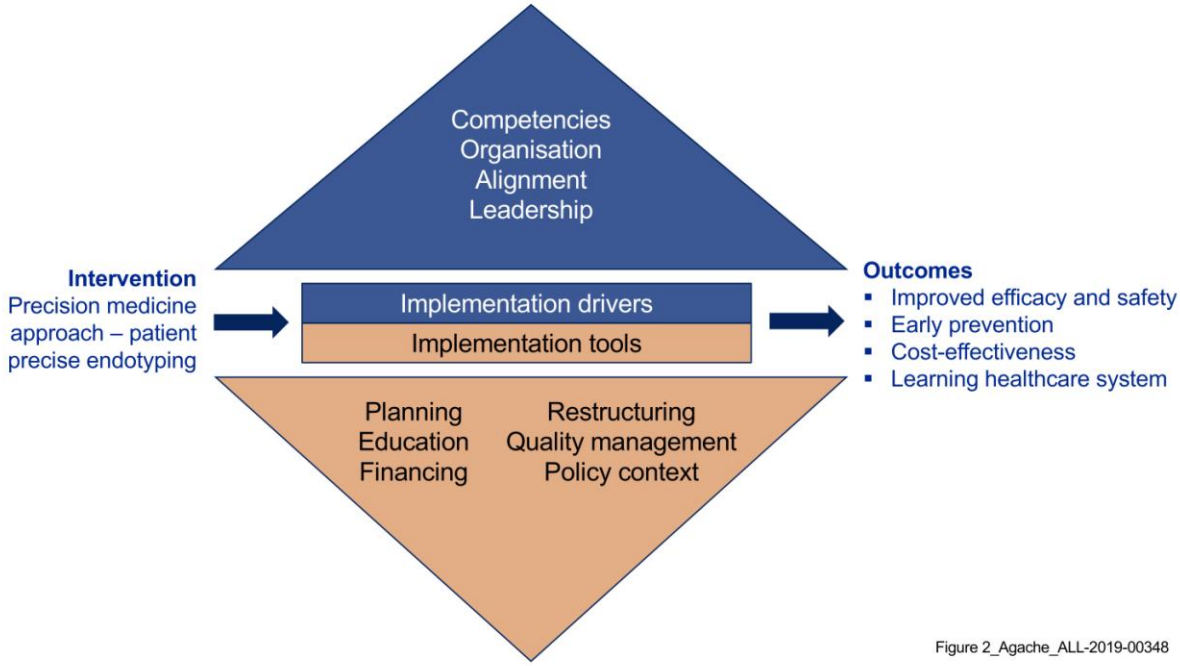


Figure 1_Agache_ALL-2019-00348



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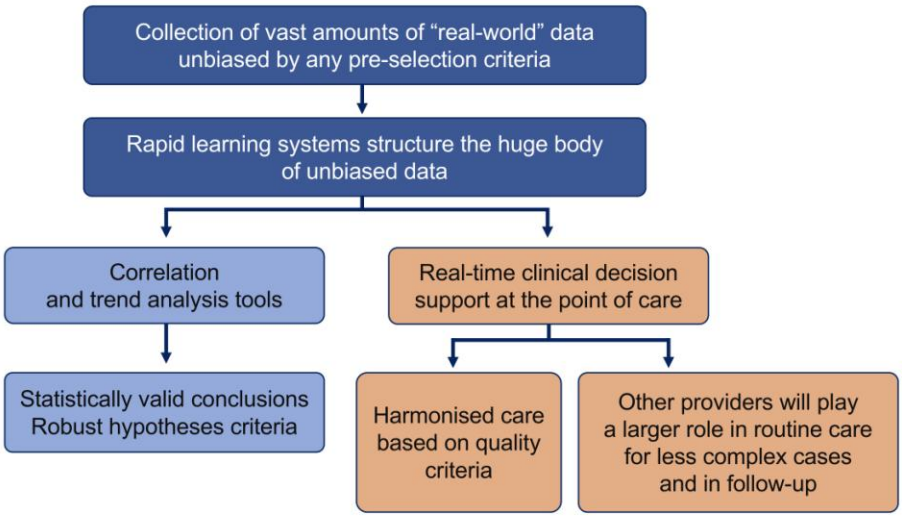

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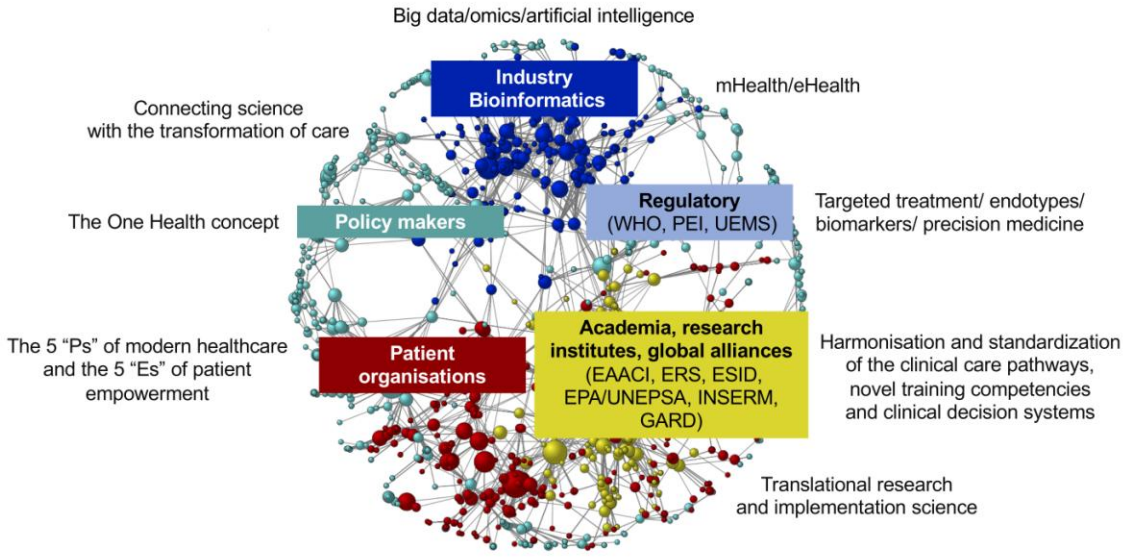

Figure 4_Agache_ALL-2019-00348